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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,504	04/13/2005	John J. Renger	21245YP	9078

210 7590 07/18/2008

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EXAMINER	
JAVANMARD, SAHAR	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
07/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,504	RENGER ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 3/13/08. Claim(s) 51-60 are pending. Claim(s) 1-50 have been cancelled. Claim(s) 51-60 have been added and are examined herein.

Response to Arguments

Applicant's arguments with respect to the 112 1st rejection of claims 33-50 has been fully considered but found not persuasive.

Applicants assert in view of the specification and the state of the art, one of ordinary skill in the art could practice the claimed invention without undue experimentation. This is not persuasive because how does one know with all the known calcium channel antagonists in the art which ones possess those properties that Applicant has claimed without undue experimentation? With the shear number of calcium channel antagonists, undue experimentation would be required in order to determine which compounds possess the calcium channel selectivity set forth by the Applicant.

Furthermore, Applicant contends that mibefradil was initially believed to be a selective T-type calcium channel antagonist, but is now admitted to potently inhibit other ion channels, including L-type calcium channels. This is not persuasive because at the

time of the invention mibefradil was known in the art to be a selective T-type calcium channel antagonist.

The 112 1st rejection is maintained for the newly added claims.

Applicant's arguments with respect to the 103(a) obviousness rejection of claims 33-50 has been fully considered but found not persuasive as Applicant is now arguing based on amended claims. The 103(a) obviousness rejection of the last Office Action has been modified below as a result of Applicant's claim amendments (cancellation of all claims originally submitted and addition of new claims 51-60)..

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for some T-type calcium channel antagonists, namely, compounds A-D, does not reasonably provide enablement for enhancing the quality of sleep, augmenting sleep maintenance and treating insomnia with any T-type calcium channel antagonist as set forth in the instant claims. The specification does not provide sufficient information that all T-type calcium channel antagonists are capable of enhancing the quality of sleep, augmenting sleep maintenance and treating insomnia. Thus, the term "T-type calcium channel antagonists" is very broad as cited in claims 51-60.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that all T-type calcium channel antagonists are capable of enhancing the quality of sleep, augmenting sleep maintenance and treating insomnia.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a method of enhancing the quality of sleep, augmenting sleep maintenance and treating insomnia with the administration of a T-type calcium channel antagonists as described in claims 33-50. The nature of the invention is complex in that it encompasses the treatment said

ailments using a wide array of compounds encompassed by the term "T-type calcium channel antagonists".

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass methods of enhancing the quality of sleep, augmenting sleep maintenance and treating insomnia by administering a wide array of compounds encompassed the term "T-type calcium channel antagonists". There are countless possible compounds encompassed by "T-type calcium channel antagonists" for the treatments claimed. The general definition "T-type calcium channel antagonists" used in the claims of the present application does not clearly define any chemical compound and is not known in the art to which it pertains. If there is support for the specific T-type calcium channel antagonists, the claims must be limited as such. The claims are therefore much broader than the enabling disclosure.

(3). Guidance of the Specification:

The guidance given by the specification as to how effective the disclosed T-type calcium channel antagonists are at treating the desired ailments is limited, in particular there are no structures provided for compounds A-C in the table on page 17 of the specification. Additionally, there is no data on how effective these compounds are at treating the desired ailments. Further, there is no selectivity data on compound A.

(4). Working Examples:

Applicant provides an example of a preclinical study on the effects of a T-type calcium channel antagonist on sleep (compound A). There is a second clinical study involving T-type calcium channel antagonists involving healthy young adults, but it is not clear which compounds were tested.

(5). State of the Art:

The most pertinent art that the Examiner is aware involves mibefradil (*AJH*, 1998), a selective T-type calcium channel antagonist. Mibefradil increases coronary blood flow, lowers peripheral resistance, blood pressure, and heart rate, but does not decrease cardiac contractility or stimulate the neuroendocrine system (page 97S).

(6). Nature and predictability of the invention

The nature of the invention is directed towards medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(7). The Quantity of Experimentation Necessary:

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each

compound as encompassed by "T-type calcium channel antagonists", the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for enhancing the quality of sleep, augmenting sleep maintenance and treating insomnia. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding sleep ailments with any T-type calcium channel antagonists, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to enhance the quality of sleep, augment sleep maintenance and treat insomnia by administration of one of the T-type calcium channel antagonists as set forth in the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, methods of enhancing the quality of sleep, augmenting sleep maintenance and treating insomnia by administering T-type calcium channel antagonists of the claims is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 51-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Branca (US Patent No. 4,808,605) in view of Snutch (WO 01/02561 A2).

Branca teaches compounds of formula I that have pronounced calcium-antagonistic and anti-arrhythmic activity and can be used as medicaments, especially for the control or prevention of angina pectoris, ischaemia, arrhythmias, high blood pressure and cardiac insufficiency. Banca specifically teaches Applicant's compound D

(disclosed in specification), [1S, 2S]-2-[2-[[3-(2-benzimidazolyl)propyl]methylamino]-ethyl]-6-fluoro-1,2 ,3 ,4-tetrahydro-1-isopropyl-2-naphthyl methoxyacetate (column 4, lines 25-26).

Branca teaches the administration of compounds of formula I to warm-blooded animals (column 15, lines 50-51) in oral form (column 15, lines 61-65).

Branca does not teach compound D as a method for reducing the number of awakenings. Furthermore, Branca does not teach the compound as possessing the selectivity properties as claimed by Applicant as set for in claim 51.

Snutch teaches T-type calcium channel encoding sequences, expression of these sequences, and methods to screen for compounds which antagonize calcium channel activity (page 1, lines 4-6).

Snutch further teaches the resulting identified compounds are useful in treating conditions where undesirable T-type calcium channel activity is present, including sleep disorders, cardiac hypertrophy and hypertension, among others (page 5, lines 8-11).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have employed compound D as taught by Branca and also used it to treated sleep disorders. The motivation, provided by Snutch, teaches that T-type calcium channel antagonists are useful in the treatment of sleep disorders. Thus one of ordinary skill in that art would expect with a reasonable degree of success that compound D would also be useful in the treatment of sleep disorders such as reducing the number of awakenings.

Additionally, evaluation of the IC50s of the compounds by voltage-clamp assay is known in the art (Fong, US Patent Number 5,484,886).

Furthermore, since the prior art discloses the same compound claimed by Applicants, absent evidence to the contrary of the selectivity properties, the prior art compound would also be expected to have the same properties as Applicant's claimed compound (i.e., the IC50s and T-type: L-type calcium channel ratios). See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting *In re Best* 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the prior art compounds would or would not have the additional functional limitation of "a selective T-type calcium channel antagonist."

Conclusion

Claims 51-60 are not allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617